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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,602	05/25/2006	Robert Boizel	MERCK-2822	4960

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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
BLAND, LAYLA D	

ART UNIT	PAPER NUMBER
1609	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,602	BOIZEL ET AL.	
	Examiner	Art Unit	
	Layla Bland	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 34-37* is/are pending in the application.

4a) Of the above claim(s) *7,12 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8-11, 13-25, 35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/25/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I, claims 1-25 in part, and election of the species (2E, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid on May 15, 2007 is acknowledged. In a telephone call dated May 24, 2007, the election of Group I was changed to Group IV so that the elected species would fall within the group. In the amendment dated May 15, 2007, claims 26-33 were cancelled and new claims 34-37 were added. Claims 7, 12 and 34 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-6, 8-11, 13-25 and 35-37 are examined on the merits herein.

In the response dated May 15, 2007, Mr. Henter traversed the restriction requirement on the basis that search burden had not been established. Because the instant application is a national stage application submitted under 35 U.S.C. 371, the Unity of Invention practice in MPEP § 1850 and MPEP § 1893.03(d) was followed, not restriction practice. Thus, the criteria for burden stated in MPEP § 803 for national applications filed under 35 U.S.C. 111(a) does not apply. (MPEP § 801)

The restriction requirement dated April 26, 2007 is still deemed proper and is therefore made FINAL.

Specification

The specification is objected to because it lacks a brief description of the drawings. Appropriate correction is required.

Claim Objections

Claims 1, 14 and 16 are objected to because of the following informalities: Claim 1 has a period after "a compound of formula (I)," in the middle of the claim. Claim 14 contains a misspelling, "nephropaty." Claim 16 contains "420 %m/L," which is presumably intended to read "420 μm/L." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8-11, 13-25 and 35-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment or prevention of hyperuricemia, the treatment of disorders associated with hyperuricemia, and for reducing the serum uric acid level of a subject, does not reasonably provide enablement for the prevention of all disorders associated with hyperuricemia. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not

'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to the treatment and/or prevention of hyperuricemia and disorders or diseases related to hyperuricemia and the reduction of serum uric acid levels in a subject via administration of a compound of formula (I). Thus, the claims taken together with the specification imply that any disorder associated with hyperuricemia may be prevented by administering a compound of formula (I).

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Pittman, et al. (American Family Physician, Vol. 59/No. 7 (April 1, 1999) teach that although hyperuricemia is a risk factor for the development of gout, the exact relationship between hyperuricemia and acute gout is unclear. Patients may have hyperuricemia without gout; and may have gout without hyperuricemia [Pathogenesis, third paragraph]. The National Institutes of Health (Questions and Answers About Gout, published March 2002, revised December 2006) teaches that gout can be caused by genetics, gender and age, weight, alcohol consumption, diet, lead exposure, health problems such as hypothyroidism, and medications such as diuretics.

(5) The relative skill of those in the art:

The relative skill of those in the art is high.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for the reduction of plasma uric acid concentration in healthy male volunteers by administration of a compound of formula (I).

However, the specification does not provide guidance for the treatment or prevention of any disease.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to the various causes of gout and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to the method of claim 1, wherein the compound of formula (I) is administered in lower than the amount used in the treatment of dyslipidemia, atherosclerosis or diabetes. The claims are indefinite

because the amount used in the treatment of dyslipidemia, atherosclerosis or diabetes is not given in the claim or the specification.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 8-11, 13-25 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brunet, et al (WO 00/39113, published July 6, 2000) in view of Chen, et al. (WO 00/47209, published August 17, 2000).

Brunet, et al. teach compounds of the same core structure as the instant application. The compounds are activators of the PPARα and PPARγ isoforms and exhibit hypolipidaemic and hypoglycaemic effects [page 2, lines 15-25]. The hypolipidaemic and hypoglycemic effect of the compounds result from their ability to activate the PPARa and PPARγ isoforms [page 33, lines 15-17]. Given as an exemplary compound [page 34, lines 12-15] and preferred species [page 10, lines 9 and 10] is Example 16b, (2E, 4E)-5-(3,3-dimethyl-7-methoxy-2,3-dihydrobenzoxepin-5-yl)-3-methylpenta-2,4-dienoic acid, which is the species which applicant has elected in the instant application. To demonstrate the antidiabetic and hypolipidaemic activity of the compounds, mice were treated via oral administration of 100mg/kg/day of the compound of example 16 [page 34, lines 21-26].

Brunet, et al. do not teach the treatment of hyperuricemia or associated disorders, or the lowering of the serum uric acid level of a subject.

Chen, et al. teach that activators of PPARγ are useful for the treatment of gout and related disorders [page 2, lines 31-33]. Chen, et al. also teach methods for the treatment of diseases associated with hyperuricemia (defined by Pittman, et al. as a serum uric acid concentration above 7 mg per dL) and methods for modulating serum uric acid levels in a subject [page 3, lines 1-5 and 23-24]. The preferred dosage for administration of a high affinity PPARγ ligand is in the range of 0.05 mg/kg to about 20 mg/kg, more preferably 0.05 mg/kg to about 2 mg/kg, most preferably 0.05 mg/kg to 0.2 mg/kg per day [page 10, lines 12-15]. Administration may be provided in single or multiple dosages [page 10, lines 19-21].

It would have been obvious to one of ordinary skill in the art to use the compounds of Brunet, et al. for the treatment of hyperuricemia and associated disorders. The skilled artisan would have been motivated to do so with an expectation of success because Chen, et al. teach that activators of PPARγ are useful for the treatment of gout and related disorders and the compounds of Brunet, et al. are PPARα and PPARγ activators. The exemplary compound of Brunet, et al. (elected species in the instant application) meets the limitations of claims 1-6, 8-11, 13-25, and 35-37. The dosages suggested by Chen, et al. are more than 90% lower than the 100 mg/kg/day used by Brunet, et al. for the study of in vivo antidiabetic and hypolipidaemic activity in mice and meet the limitation of claim 24.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Bland whose telephone number is (571) 272-9572. The examiner can normally be reached on M-R 8:00AM-5:00PM UST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ldb

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER